West Nile Virus for Clinicians, May 2003

During the late summer of 2002, a woman traveled from her home in Western Washington to Michigan, and on her return developed rash, fever and a headache. While in Michigan, she was bitten several times by mosquitoes. An alert dermatologist evaluating her obtained serum for West Nile virus (WNV) antibody testing. She recovered quickly and her illness was subsequently confirmed as travel-associated WNV infection. As of May 1, 2003 there have not yet been any reported human cases of WNV acquired in the Washington, however we expect that this summer (2003) WNV infection will be diagnosed.

Epidemiology: The 2002 outbreak of West Nile virus (WNV) infection in the United States was the largest recorded outbreak of arthropod-borne illness in the Western Hemisphere. WNV, a flavivirus, is closely related to viruses that cause Japanese encephalitis, yellow fever, St. Louis encephalitis (SLE) and dengue. WNV can cause disease in humans, horses, birds, and other vertebrates. In the fall of 2002, WNV infection was detected in a crow, a raven, and two horses from counties in eastern and western Washington. WNV is expected to become more widely established in Washington state during 2003.

Human WNV infection in the United States was first reported in New York City in 1999. Before 1999, WNV was found only in the Eastern Hemisphere. Between 2000 and 2002, WNV spread throughout the Northeast and mid-Atlantic U.S., to the South, and the Midwest. During 2002, more than 4100 human cases of WNV were reported from 39 states and DC, with the highest concentration of human cases in the South and Midwest. A single human case was reported in California.

Approximately 28% of the reported cases during 2002 had a self-limited mild febrile WNV illness, and the balance had viral meningitis, encephalitis, or one of the more rare syndromes. There were 263 WNV associated fatalities during 2002. WNV infection peaked in humans during late August, with onsets ranging from May to December. As of March 1, 2003 WNV activity (infection in birds, mosquitoes, horses, or humans) has been reported in 43 states, including eastern and western Washington. The Center for Disease Control and Prevention CDC) lists reported human WNV case counts by state: http://www.cdc.gov/od/oc/media/wncount.htm

In Washington, human cases of western equine encephalitis (WEE) and SLE virus infection have been identified in the past. Most of the documented cases occurred in central Washington, with the last reported case in Chelan County in 1982.

Transmission: WNV is transmitted primarily by bites of infected mosquitoes. Mosquitoes acquire WNV after feeding on virus-infected birds. WNV is not transmitted between humans by direct contact. However, several new modes of transmission were identified during the 2002 epidemic:

- Several human infections involved recipients of organ transplants and blood transfusions (1,2). The virus was transmitted in organs and units of plasma, red blood cells, and platelets.
- The virus was found in the breast milk of a nursing mother whose infant developed antibodies without clinical illness (3).

- One case of transplacental transmission was documented after acute maternal infection during the late second trimester. The infant had cerebral abnormalities at birth (4).
- Two laboratory-acquired WNV infections were reported during 2002. Both cases followed percutaneous inoculation (scalpel and needlestick) of infectious materials (5).

Incubation period and clinical signs: The incubation period is three to 15 days. Knowledge of the spectrum of WNV infection increased substantially during 2002, but the complete range of illness is still unknown. Based on serologic screening in endemic communities, the vast majority of WNV infections in humans are asymptomatic. Approximately 20% of infected individuals experience a mild, self-limiting febrile illness called West Nile fever, lasting three to six days. Symptoms may include fatigue, anorexia, nausea, vomiting, eye pain, headache, muscle pain, weakness, and rash.

Severe WNV infection with acute meningitis and/or encephalitis occurs in less than one percent of infected individuals. Associated symptoms may include fever, pronounced weakness, nausea, vomiting, headache, altered mental status, diarrhea, rash, stiff neck, cough, and muscle aches. The case-fatality rate for WNV encephalitis is 5 to 15%; individuals older than 70 years of age have a much higher risk of fatal outcome.

Acute flaccid paralysis (AFP) is known to be a clinical manifestation of WNV infection. AFP presents as an asymmetrical poliomyelitis-like syndrome without fever or other neurological symptoms (6). Differential diagnosis includes Guillain-Barré syndrome and stroke. Health care providers are encouraged to consider testing for WNV infection in patients that present with AFP.

Other syndromes recently associated with WNV infection include movement disorders with static, kinetic tremors severe enough to impede activities; myoclonus of the upper extremities with facial involvement; Parkinsonism (postural instability, bradykinesis), and rhabdomyolysis

Long-term or permanent sequelae, including persisting neurological deficits, are not uncommon among those who have experienced severe WNV infection.

Among patients in recent outbreaks, abnormal white blood cell and cerebral spinal fluid (CSF) profiles indicate the presence of a viral infection. Thirty percent of patients show enhancement on MRI imaging of the brain. However, no routine laboratory or radiological findings are specific for WNV infection.

Diagnosis: Diagnosis of WNV infection is based on a epidemiologic and clinical findings along with laboratory testing. WNV infection should be strongly considered in adults over 50 years of age who develop unexplained viral encephalitis or meningitis in summer or early fall and in cases of acute flaccid paralysis. Suspicion of WNV infection should be further raised when there is evidence of human or animal illness locally. Obtaining information on a patient's occupation, pregnancy and breast-feeding status, recent travel history, blood donations and transfusions, and recent organ transplantation is important.

Laboratory testing: An enzyme-linked immunosorbent assay (ELISA) to detect IgM and IgG antibodies in serum and CSF is available for hospitalized patients through the

Washington State Public Health Laboratories (PHL). Serum or CSF should be obtained at least 8 days after the onset of symptoms. If convalescent serum is collected it should be obtained 2-4 weeks after the acute sample. ELISA assays for WNV may cross-react with antibody from yellow fever or Japanese encephalitis vaccination or from infection caused by St. Louis encephalitis (SLE) virus, yellow fever virus, or dengue. For diagnosis of mild WNV fever cases, testing is available through commercial laboratories. **Local health jurisdictions must be contacted prior to submitting specimens for testing at the WA Public Health Laboratories.**

Treatment: There is no specific recommendation for management of WNV other than supportive care. Patients with severe disease may require intensive care hospitalization. Ribavirin and interferon alpha-2b have shown some activity against WNV in vitro. An ongoing controlled trial of interferon alpha 2b in adult patients with encephalitis and other neurological syndromes is being conducted through New York Hospital; more information on the trial is available at http://www.nyhq.org/posting/rahal.html. There is no WNV vaccine for humans available at present.

Prevention: Everyone should take should take precautions to avoid mosquito bites, including use of appropriate mosquito repellents or staying indoors at dusk and dawn, when mosquitoes are most active. This is particularly important for persons at increased risk for adverse outcomes following WNV infection.

Reporting: Both suspected and confirmed cases of WNV fever and WNV infection are immediately reportable in Washington. To report a case, contact your local health jurisdiction or call Washington State Department of Health, Communicable Disease Epidemiology at
(206) 361-2914 or (877)-539-4344. The timely identification of persons with acute WNV is important and will trigger public health responses to reduce the risk of additional human infections.

References:

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2. Public Health Dispatch: Investigations of West Nile Virus Infections in Recipients of Blood Transfusions Morbidity and Mortality Weekly Report (MMWR) November 1, 2002 / 51(43);973-974
3. Possible West Nile Virus Transmission to an Infant Through Breast-Feeding --- Michigan, 2002 Morbidity and Mortality Weekly Report (MMWR) October 4, 2002 / 51(39);877-878
4. Intrauterine West Nile Virus Infection --- New York, 2002 Morbidity and Mortality Weekly Report (MMWR) December 20, 2002 / 51(50); 1135-1136
5. Laboratory-Acquired West Nile Virus Infections --- United States, 2002 Morbidity and Mortality Weekly Report (MMWR) December 20, 2002 / 51(50); 1133-1135 1129-1133
6. Acute Flaccid Paralysis Syndrome Associated with West Nile Virus Infection --- Mississippi and Louisiana, July--August 2002
September 20, 2002 / MMWR 51(37); 825-828

Additional clinical information is available in: Petersen LR and Marfin AA, "West Nile Virus: A Primer for the Clinician [Review]," *Annals of Internal Medicine* (August 6) 2002: 137:173-9.